II. RESPONSE TO OFFICIAL ACTION

A. Status of the Claims

Claims 10, 22, 28, 32, 34, 36, 38, 40-43, 45-50, 107, 111, 113, 115, 117, and 121-125 are pending in the case, were rejected in the action and are presented herein for reconsideration. The claims have been amended herein. Support for the amendments is found in the claims as filed.

B. Claim Objections

The Action objects to claims 43, 46-47 and 49-50 as in multiple dependent form for use of the term "the recombinant construct" instead of "said recombinant construct" in reference to the recombinant construct of claim 22. In response, Applicants note that the claims have been amended as suggested to recite "said recombinant construct" and therefore the objection is now believed moot. Removal of the objection is thus respectfully requested.

C. Rejections Under 35 U.S.C. §112, First Paragraph- Written Description

The Action rejects claims 10, 22, 28, 34, 36, 38, 40-43, 45-50, 107, 111, 115, 117 and new claims 123-125 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. For example, it is asserted that written description is lacking for polynucleotides defined as having at least 80% identity to SEQ ID NO:4 and sequences that hybridize to SEQ ID NO:4. In particular, it is asserted that there no examples of such sequences and that the common features of such sequences are not provided.

Applicants respectfully traverse as the current claims are fully supported by a written description in the specification demonstrating possession of the claimed invention. In particular, the current claims define a scope of subject matter with full support in the specification. For

example, the claims require sequences encoding the polypeptide of SEQ ID NO:5 or having at least 80% sequence identity or hybridizing under stringent conditions to SEQ ID NO:4. The claims also recite nucleic acids encoding a plant lecithin: cholesterol acyltransferase-like polypeptide. Applicants were in possession of this subject matter based on the description of SEQ ID NOs:4 and 5 and further descriptions in the specification, as it is well settled that an Applicant need not limit the claims to that subject matter having *ipsis verbis* description. *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (stating that the written description requirement does not require an applicant to "describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (citations omitted)). Further, written description must be reviewed from the perspective of one of skill in the art at the time the application is filed. *Wang Labs., Inc. v. Toshiba Corp.*, 993 F.2d 858, 863 (Fed. Cir. 1993).

In regard to the foregoing Applicants note that FIG. 1 of the specification specifically ***shows the conserved regions*** of the *Arabidopsis* LCAT2 (SEQ ID NO:5) relative to other *Arabidopsis* LCAT-like sequences and even distantly related sequences in yeast, humans and rats. As can be seen, the *Arabidopsis* LCAT2 includes a number of ***highly conserved regions***. In addition, the specification describes the isolation of other related plant sequences. This information alone provides more than an adequate structural description of the entire scope of the claimed invention and demonstrates possession of the invention in compliance with the written description requirement. As explained in the specification, it was routine in the art as of the filing date to make silent changes to a given polypeptide while retaining activity. These procedures are described in the specification. For example, changes can be made to coding sequence without even changing the polypeptide sequence by altering codon usage. The

Detailed Description of the Invention also describes the use of techniques for altering the amino acid residues of a polypeptide while retaining or even improving enzymatic activity. For example, it is explained that conservative amino acid substitutions can be made by substitution with residues having like characteristics, including hydropathic index. It also explained that the relative hydropathic character of amino acids contributes to the secondary structure of the resultant protein and thus interaction of the protein with molecules such as enzymes, substrates, receptors, DNA, antibodies, antigens, etc. Based on hydrophobicity and charge characteristics, each amino acid has been assigned a hydropathic index and these are given in the specification. Those amino acids sharing a similar score may be selected and substituted for one another based on the known hydropathic indices.

It is also explained in the specification that like amino acids can be substituted based on hydrophilicity, and that this is described in U. S. Patent No. 4,554,101. Values for assessing hydrophilicity have been assigned and can be used for selecting an amino acid for substitution, as described in the specification. It is also well known that amino acid substitutions can be based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, etc. Use of these changes is also described, as further outlined in the response to the enablement rejection below. There is, therefore, no basis in law or science to attempt to limit Applicants to any less than what is being claimed.

With respect to the assertion at page 3, middle paragraph of the Action that formation of sterol esters in transformed cells is shown only with respect to SEQ ID NO:6 and SEQ ID NO:8, Applicants note that the current claims are directed to SEQ ID NOs:4 and 5 and related sequences and that Example 7 shows that such an LCAT2 gene was expressed in plants yielding a significant increase in the oil level in seed from T2 plants. Specification at Fig. 5 and Table 2.

Applicants also note that LCAT2 is described in the cited Noiriel reference as possessing sterol acyltransferase activity (see p.3757 2nd col; and refs 48a, 48b cited therein). The Noiriel reference therefore does not in any way teach that the presently claimed LCAT2 and related sequences lack acyltransferase activity. On the contrary, Noiriel *et al.* state that LCAT2 is a sterol acyltransferase. Additionally, the specification at page 49, lines 5-17; figure 5; and table 2, pages 50-51 describes use of LCAT2, encoded by SEQ ID NO:4, in creating transgenic plants with increased oil content. This is also noted by the Action at page 5, fourth paragraph.

In view of the foregoing and currently claimed subject matter, Applicants submit that the rejection is now moot and respectfully request that it be withdrawn.

D. Rejections Under 35 U.S.C. §112, First Paragraph - Enablement

The Action rejects claims 10, 22, 28, 34, 36, 38, 40-43, 45-50, 107, 111, 115, 117, and 123-125 under 35 U.S.C. §112, first paragraph, as lacking enablement. In particular, the Action acknowledges that the claims are enabled for recombinant vectors comprising SEQ ID NO:4 or encoding SEQ ID NO:5, but asserts that enablement has not been provided for all sequences at least 80% complimentary to SEQ ID NO:4 or that hybridize to SEQ ID NO:4 and provide altered oil production. It is thus alleged that the specification does not enable the practice of the full scope of the claims.

In response, Applicants note that the full scope of currently claimed subject matter is enabled. While the claims, in addition to covering nucleic acids encoding the polypeptide sequence of SEQ ID NO:5 and comprising SEQ ID NO:4, cover sequences that hybridize with these sequences under specified stringent conditions or have at least 80% sequence identity to SEQ ID NO: 4, at most routine experimentation would be required for one of skill in the art to

make and use the full scope of claimed subject matter. FIG. 1 of the specification in particular demonstrates that the *Arabidopsis* LCAT2 (SEQ ID NO:5) contains highly ***conserved regions*** relative to other *Arabidopsis* LCAT-like sequences and even relative to distantly related sequences in yeast, humans and rats. As these regions are ***shown in the specification***, it would at most require routine experimentation to alter non-conserved residues to obtain other sequences encoding polypeptides with the same activity and having no more than 80% identity to SEQ ID NO:4 or 5. It was routine and well known in the art as of the filing date to create sequence variants comprising silent nucleic acid mutations or those leading to conservative amino acid changes such that the activity of the encoded polypeptide is maintained. Creation of sequence variants requires only routine substitution of the starting nucleic acid molecules, which is fully described in the specification and well known in the art.

The Detailed Description of the Invention, in particular, describes the techniques one of skill in the art would use to change amino acids of a polypeptide encoded by any of the claimed nucleic acids while retaining or even improving enzymatic activity. For example, it is explained in the Detailed Description that conservative amino acid substitutions can be made by substitution of a residue with another having like characteristics. It is explained that one criteria that may be used in this regard is the hydropathic index of amino acids and that the significance of hydropathic amino acid index in conferring biological function of a protein has been discussed by Kyte and Doolittle (*J. Mol.Biol.*, 157: 105-132, 1982). It is noted that the relative hydropathic character of amino acids contributes to the secondary structure of the resultant protein and thus interaction of the protein with molecules such as enzymes, substrates, receptors, DNA, antibodies, antigens, etc. Based on hydrophobicity and charge characteristics, each amino acid has been assigned a hydropathic index and these are given in the specification. Those amino

acids sharing a similar score may be selected and substituted for one another based on the known hydropathic indices.

It is also explained in the specification that like amino acids can be substituted based on hydrophilicity, and that this is illustrated in U. S. Patent No. 4,554,101. Values for assessing hydrophilicity have also been assigned and can be used for selecting an amino acid for substitution, as described in the specification. It is also known that amino acid substitutions can be based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, etc. In this regard the specification explains that amino acids can be divided into the following four groups: (1) acidic amino acids; (2) basic amino acids; (3) neutral polar amino acids; and (4) neutral nonpolar amino acids, and that representative amino acids within these various groups include, but are not limited to: (1) acidic (negatively charged) amino acids such as aspartic acid and glutamic acid; (2) basic (positively charged) amino acids such as arginine, histidine, and lysine; (3) neutral polar amino acids such as glycine, serine, threonine, cysteine, cystine, tyrosine, asparagine, and glutamine; and (4) neutral non-polar amino acids such as alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine. Similarities within these groups can also be used to substitute an amino acid.

The specification therefore fully enables the claim scope based on the provision of SEQ ID NO:4 and SEQ ID NO:5. While some routine mutagenesis may be required to generate sequence variants, this would not be undue because the techniques that would be used are targeted, well known in the art, and fully described in the specification. The biological activity of any given sequence generated could routinely be confirmed by the transformation of plants

with plant transformation vectors comprising the sequences followed by measurement of seed oil quantity and/or quality using the methodology of working Examples 4, 6 and 7.

Regarding claims covering transgenic plants, the experiments in the specification, e.g. Example 4, describe the creation of transgenic plants comprising an LCAT2 transgene. Further, Example 7 shows that, as demonstrated in Figure 5 and Table 2, there was a significant increase in the oil level in seed from T2 plants expressing the LCAT2 gene. This increase in oil was seen in plants when LCAT2 was driven by either the 35S constitutive promoter or the seed-specific napin promoter. These plants are representative of the claimed sequences, as the claims are limited to sequences of close structural relation, as demonstrated above. Again, it was routine as of the filing date to make conservative modifications altering polypeptides without destroying enzymatic activity and the working examples show the corresponding activity and phenotypic effect.

The Action also asserts that a likely candidate for lecithin:cholesterol acyltransferase showed phospholipase A1 activity (Noiriel *et al.*), and thus the specification is not enabling for any lecithin:cholesterol acyltransferase-like sequence to be confirmed as an acyltransferase. In response, Applicants first note that the present claims relate to the nucleic acid and amino acid sequences of SEQ ID NO:4-5, *i.e.*, for LCAT2, rather than the AtLCAT3 protein described by Noiriel as possessing phospholipase activity. The working examples further show activity for this sequence. In addition, the LCAT2 and LCAT3 genes are structurally distinct, sharing less than approximately 48% identity at the DNA level and 22% identity at the protein level (*e.g.* when SEQ ID NO:4 is compared to SEQ ID NO:6). Thus, no conclusions can be made as suggested with respect to LCAT2-like sequences.

In sum, Applicants have affirmatively demonstrated enablement of the claims and no basis to doubt the enablement has been provided. Removal of the rejection is thus respectfully requested.

E. Rejections Under 35 U.S.C. §112, Second Paragraph

(1) In claim 43 "a polypeptide" is said to lack antecedent basis. In response, Applicants note that the term has been replaced with "the polypeptide". It is thus believed that the rejection is moot and removal thereof is respectfully requested.

(2) In claim 49, it is asserted that the limitation "a plant" lacks antecedent basis. In response, Applicants note that the term has been replaced to recite "the plant". It is believed that the rejection is moot and removal thereof is respectfully requested.

F. Rejections Under 35 U.S.C. §102(a)

The Action rejects claims 1, 5-7, 10-11, 22, 26, 28, 30, 32, 34, 36, 38, and 40 under 35 U.S.C. 102(a) as being anticipated by Federspiel *et al.* In particular, it is asserted that Applicants' previous arguments stating that the claimed coding sequences are operably linked to a heterologous promoter were not persuasive because the claim does not state that the coding sequence is operably linked to the heterologous promoter and rather only that the isolated nucleic acid sequence comprises the polynucleotide that encodes the polypeptide. It is thus asserted that the claims still read upon the bacterial artificial chromosome, isolated by Federspiel *et al.* It is stated that amending the claim to recite "wherein the isolated polynucleotide encoding said polypeptide is operably linked to a heterologous regulatory sequence functional in plants" would overcome the rejection. In response Applicants note that claim 10 has been amended to explain

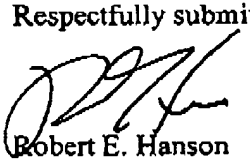
that the claimed isolated nucleic acid sequence comprises a coding sequence and that the coding sequence is operably linked to the heterologous regulatory sequence. The suggestion in the action was not followed verbatim to ensure that the claim was materially consistent with all elements of the claims. It is believed that the amendment addresses all of the Examiner's concerns and that the rejection is now moot. Removal of the rejection is thus respectfully requested.

Because every element of the presently amended claims is not present in the reference, the claims are not anticipated by Federspiel. M.P.E.P. § 2142. In view of the above, Applicants respectfully request that the rejection be removed.

G. Conclusion

In light of the foregoing, Applicants submit that the case is in condition for allowance, and an early indication to that effect is earnestly solicited. The examiner is invited to contact the undersigned (512)536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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